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IMPORTANCE OF INITIAL MANAGEMENT

OF PERSONS INTERNALLY CONTAMINATED WITH RADIONUCLIDES

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IMPORTANCE OF INITIAL MANAGEMENT OF PERSONS INTERNALLY CONTAMINATED WITH RADIONUCLIDES*

The first one or two hours after a radiation accident during which a radionuclide has been inhaled, ingested, or injected, may be the crucial time for effective treatment. First aid following internal contamination, just like first aid following a traumatic injury, may determine the prospects for success in a total treatment program. If no action is taken by plant health personnel and referral has to be made to a distant medical center, many hours may be lost and a golden opportunity missed.

Following internal contamination there is usually a period of time before the radionuclide has been absorbed, transported and taken up by tissue cells. The absorption from the lung, gut, or wound, can sometimes be reduced by chemical manipulation in the GI tract, or by hastening the passage of the material through the body. Alkalizing the stomach may cause the formation of relatively insoluble hydroxides[1] or will at least keep the pH high enough to reduce solubility of some metal salts. Metals such as copper,[2] iron,[3] or plutonium are generally more available for later absorption after spending some time in the acid milieu of the stomach. With chromium, the opposite is true. Acid gastric juice reduces hexavalent chromium to the poorly absorbed trivalent ion.[4] The administration of a cathartic such as magnesium sulfate will shorten the intestinal transit time, thereby reducing absorption and radiation exposure to the gut wall and nearby tissues. Once absorbed, uptake can be reduced by the use of blocking agents, isotopic dilution, or chelating agents.

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A blocking agent is a chemical which saturates a tissue with a non-radioactive element, thereby reducing the uptake of the radionuclide. Isotopic dilution refers to the administration of large quantities of the stable isotope of the radionuclide so that on a statistical basis alone, the opportunity for incorporation of atoms of the radionuclide is lessened. With isotopic dilution, it is desirable to get the stable isotope into the system quickly, and when possible, in a chemical form that is more easily absorbed and incorporated than the radioisotope. A special form of dilution therapy, sometimes called displacement therapy, refers to the use of a non-radioactive element of a different atomic number to compete with the radionuclide. An example would be the use of calcium to compete with radiostrontium or stable iodine to reduce the thyroidal uptake of radiotechnetium. Chelating agents bind metals into complexes, preventing tissue uptake and allowing urinary excretion.

Highly selective uptake of any radionuclide, for example ^{131}I, into the thyroid gland or ^{239}Pu into the bone and liver, should be avoided if possible. Accidental inhalations or injections of ^{131}I may occur following a nuclear reactor accident since it is a prominent early fission product, or during the manufacture or misadministration of the radiopharmaceutical. Inhaled iodine reaches equilibrium with body fluids in about 1/2 hour and approximately 30 percent of the uptake is deposited in the thyroid. One hundred mg of stable iodine, if given within two hours or less after exposure, will reduce the uptake by the thyroid gland by about 90 percent.[5] Stable iodine given as late as six hours after exposure will reduce uptake by about 50 percent and begun as late as 24 hours will shorten the biological half-life.

If given promptly, diethylenetriaminepentaacetic acid (DTPA) will greatly reduce the uptake of absorbed ^{239}Pu into the skeleton. Smith[6] has shown that

in pigs, whose metabolism of Pu is similar to humans, the skeletal retention of plutonium was reduced by a factor of 10 over controls as a consequence of DTPA treatment one hour following injection of 25 μCi of ^{239}Pu citrate. Eighty-three percent of the plutonium was harmlessly excreted in the urine.

The uptake of some of the actinides is remarkably rapid. One hour after injection of soluble ^{241}Am or ^{242}Cm only three to ten percent of the dose was still circulating and deposition in bone was 76 percent complete.[7] DTPA, to be maximally effective, has to be administered within the first 15-45 minutes after inhalation or injection of a soluble actinide compound.

Once uptake of a radionuclide has occurred, there is often little one can do but patiently wait for metabolism and excretion as well as physical decay to occur. Chelating agents such as EDTA, DTPA, BAL, penicillamine, or deferoxamine are sometimes useful after uptake has occurred, but their effectiveness is greatly reduced.

Table 1 below contains a list of some commonly used radionuclides and medications useful in preventing their uptake. The reported effectiveness of the treatment is also included when known. In addition to these medications, there may be other chemical or dietary manipulations which could be useful. A list of a few possibilities appears in Table 2. The agents in Table 1 or 2 must be administered by a physician familiar with possible contraindications or adverse reactions. With further study, effectiveness and safety of the agents in Table 2 could be determined in animal systems and their possible application to human accident cases could be determined.

In the management of internal contamination, medical action, even though of only modest effectiveness, has an additional psychotherapeutic effect. The physician who knows something about the absorption and metabolism of a

radionuclide and is able to prescribe a prompt course of action inspires confidence. If he seems helpless and covers his ignorance by vague reassurements, he may only increase anxiety. His therapy, of course, must do no harm and should have some reasonable promise of benefit.

In reviewing both Tables 1 and 2, the need for preplanning in an accident should be obvious. In order to administer any of these agents, they must be immediately available. In locations where only a small number of radionuclides are used, there should be no problem in stocking an appropriate supply in the medical department or pharmacy. In research laboratories and hospitals, where a wide variety of radionuclides may be used, keeping all possibly useful items on hand may be difficult. Regardless, careful preplanning should lead to better preparedness. Too few users of radionuclides think an accident will ever happen. If and when it does, however, they will expect the occupational medical department to be completely prepared.

SUMMARY

The first one to three hours following a radiation accident during which internal contamination occurs provide the best and perhaps the only opportunity for preventing uptake of radionuclides. By using chemical manipulation in the GI tract or by hastening the material through the body, absorption can be reduced. Once absorbed, uptake in specific tissues can often be prevented by blocking agents, isotopic dilution or chelating agents. In order to supply prompt treatment, the medical department must have a well-defined action plan based on knowledge of the plant or laboratory operations, the radionuclides used, and medications required.

Table 1

MEDICATIONS USEFUL IN PREVENTING UPTAKE OF RADIONUCLIDES

RADIONUCLIDE	ROUTE OF ENTRY	MEDICATION	DOSE*	EFFECTIVENESS	COMMENTS
^{241}Am	Inhalation ** Injection	DTPA	1 gm IV in 250 ml isotonic saline or 5% dextrose in water. May also be given as aerosol.[10]	In humans, 50% of body burden removed, even when therapy long delayed. In rats, DTPA 1 day after administration of ^{241}Am reduced bone content to 50% of control value.	Ref. 8,9
^{252}Cf	Inhalation Ingestion Injection	DTPA	1 GM IV in 250 ml isotonic saline or 5% dextrose in water. May also be given as aerosol.[10]	Early aerosol chelation with DTPA of estimated 20-30 nCi and catharsis with Fleet's Phospo-Soda ® reduced uptake to below detectable level in 75 days.	Ref. 11
^{144}Ce and Rare Earths to Lutetium	Inhalation Ingestion Injection	DTPA	1 gm IV in 250 ml isotonic saline or 5% dextrose in water. May also be given as aerosol.[10] Irrigate wound with 1 gm solution as needed.	When rare earths promptly complexed with DTPA they are almost entirely excreted.	Ref. 12
^{137}Cs	Inhalation Ingestion	Prussian Blue***	1 gm initially, .5 gm at 4 hrs & .5 gm at 8 hrs.	If given within 10 minutes, reduces absorption from gut by 40%.	Ref. 13
		Bio-Rex 40®	Not determined yet for humans.	As effective as Prussian Blue in rats. Resin should be non-toxic in humans since insoluble in water and dilute HCl.	Ref. 14

*Oral administration unless otherwise indicated.
**Inhalation of soluble or insoluble materials has an ingestion component due to mucociliary clearance.
***Not absorbed from gut. Acts as exchange resin. May be made by mixing 0.5 molar solutions of $FeCl_3$ and $K_4[Fe(CN)_6]$ solutions in the ratio 4:3, removing KCl by washing precipitate. See Reference 13.

Table 1 (Cont'd)
Medications Useful in Preventing Uptake of Radionuclides

RADIONUCLIDE	ROUTE OF ENTRY	MEDICATION	DOSE	EFFECTIVENESS	COMMENTS
^{242}Cm	Inhalation	DTPA	1 gm IV in 250 ml isotonic saline or 5% dextrose in water. May also be given as aerosol.[10]	Appeared to have prevented uptake following inhalation exposure. Beneficial when given promptly. Not effective after fixed in tissue.	Ref. 15 Ref. 16
^{3}H	Inhalation Ingestion Injection	Water	1-2 liters initially, continue to force fluids (5-10 liters/day) for 7-14 days. 12.8 liters per day.	^{3}H rapidly incorporated into body water. Isotopic dilution. Excretion of ^{3}H can be increased 10-20 times by prompt treatment. Half-time of body water reduced from 11.5 days to 2.4 days.	Ref. 17 Ref. 18
^{131}I	Inhalation Ingestion Injection	Potassium iodide (Lugol's Solution)	100 mg 2-3 drops in glass of water.	Reduces uptake by thyroid by 90% if given within 2 hours.	Ref. 5,19
^{140}La	Inhalation Injection	DTPA	1 gm IV in 250 ml isotonic saline or 5% dextrose in water. May also be given as aerosol.[10]	10 times more effective than EDTA. If given immediately might increase excretion from <2% to ~60%.	Ref. 20
^{210}Pb	Inhalation Ingestion Injection	Calcium disodium EDTA (Versenate®, Riker) Penicillamine (Cuprimine®, Merck, Sharp & Dohme)	1 gm IV in 250-500 ml isotonic saline or 5% dextrose in water. See directions on pkg. 500 mg/24 hrs. Give on empty stomach.	Principal use in nonradioactive lead poisoning.	Ref. 21 Ref. 22

Table 1 (Cont'd)
Medications Useful in Preventing Uptake of Radionuclides

RADIONUCLIDE	ROUTE OF ENTRY	MEDICATION	DOSE	EFFECTIVENESS	COMMENTS
^{203}Hg	Ingestion Injection	Penicillamine (Cuprimine®, Merck, Sharp & Dohme)	See directions on pkg. 500 mg/24 hrs. Give on empty stomach.	Reported for rats only. Half-times of both components of excretion curves significantly shortened by 50 mg dose.	Ref.22
^{32}P	Inhalation Ingestion	Phosphorus (Neutraphos®, Willen)	2 capsules in glass water.	Isotopic dilution. 4 capsules supply 1 gm of phosphorus.	
^{239}Pu, ^{238}Pu	Inhalation	DTPA	1 gm IV in 250 ml isotonic saline or 5% dextrose in water. May also be given as aerosol.[10]	Reduced uptake by factor of 10 when given in first hour.	Ref. 6
^{210}Po	Inhalation Ingestion Injection	Dimercaprol (BAL)	2.5 mg/kg IM 4 times a day for 2 days; 2 times/day on 3rd day, then once daily for 10 days as needed.	Dose rate to spleen in rats from oxathiol, a closely related compound, was 6.5-11.6% of dose-rate in untreated animals.	Ref.23
^{143}Pm	Injection	DTPA	1 gm IV in 250 ml isotonic saline or 5% dextrose in water. May also be given as aerosol.[10]	When DTPA given within 30 minutes, body content reduced to 14% control.	Ref.24
^{86}Rb	Inhalation Ingestion	Chlorthalidone (Hygroton®, U.S.V.)	50 mg orally per day.	More than doubled excretion.	Ref. 25

Table 1 (Cont'd)
Medications Useful in Preventing Uptake of Radionuclides

RADIONUCLIDE	ROUTE OF ENTRY	MEDICATION	DOSE	EFFECTIVENESS	COMMENTS
^{46}Sc	Inhalation Injection	DTPA	1 gm IV in 250 ml isotonic saline or 5% dextrose in water. May also be given as aerosol.[10]	Increases urinary excretion 20-30 times	Ref. 26
^{85}Sr, ^{89}Sr,	Inhalation Ingestion	Sodium alginate " " (Gaviscon®, Marion Labs)	10 grams 1.5 gm Chew 5-10 tabs stat, 2-4 every 2-4 hrs for 24 hours.	Decreases absorption from gut by a factor of 8-10 Decreases absorption from gut by a factor of 2. Not reported. Dose based on extrapolation from sodium alginate experience. See references.	Ref. 27,28
	Ingestion Inhalation	Aluminum phosphate gel (Phosphajel®, Wyeth)	100 ml stat 40 ml every 1-2 hrs depending on route of entry.	Reduces absorption from gut by 87%	Ref. 29
	Ingestion Inhalation	Aluminum hydroxide (Amphojel® Susp., Wyeth)	65 ml stat 40 ml every 1-2 hours depending on route of entry.	Reduces absorption from gut by 50%	Ref. 30
	Ingestion Inhalation	Calcium carbonate	Chew 2, 600-mg tabs every hour depending on route of entry.	Less effective than other methods.	
^{99}Tc	Inhalation Ingestion Injection	Potassium iodide (Lugol's solution	100 mg 2-3 drops in glass of water.	Reduces uptake by thyroid.	
^{90}Y	Inhalation Injection	DTPA	1 gm IV in 250 ml isotonic saline or 5% dextrose in water. May also be given as aerosol.[10]	Increases urinary excretion from 5% in 24 hrs to 48% in 24 hours.	Ref. 31

Table 1 (Cont'd)
Medications Useful in Preventing Uptake of Radionuclides

RADIONUCLIDE	ROUTE OF ENTRY	MEDICATION	DOSE	EFFECTIVENESS	COMMENTS
^{65}Zn	Inhalation Ingestion Injection	DTPA	1 gm IV in 250 ml isotonic saline or 5% dextrose in water. May also be given as aerosol.[10]	Increases urinary excretion 30 times over non-treated.	Ref. 31

Table 2

MANIPULATIONS POSSIBLY USEFUL IN PREVENTING

UPTAKE OF RADIONUCLIDES

RADIONUCLIDE	ROUTE OF ENTRY	MEDICATION OR DIETARY MANIPULATION	MECHANISM	COMMENTS
^{51}Cr	Inhalation Ingestion	Avoid antacid.	Hexavalent chromium is better absorbed than trivalent Cr. Gastric acid reduces hexavalent Cr to trivalent Cr.	Ref. 4
^{60}Co	Inhalation Ingestion Injection	Vitamin B-12	Isotopic dilution.	
^{64}Cu	Inhalation Ingestion	$CaCO_3$ and FeS	Increases pH in stomach and forms CuS which is not absorbed.	Ref. 32
		Zinc and molybdenum	Depresses copper absorption.	Ref. 33
^{59}Fe	Injection Ingestion Inhalation	Raise pH of stomach with vigorous antacid therapy	Inorganic Fe forms complexes with normal gastric juice at low pH which remain soluble in higher pH of duodenum where iron absorbed.	Ref. 3
		Phytates	Reduce absorption.	Ref. 34
		DTPA	Chelating agent.	Ref. 35
		Deferoxamine mesylate	Chelating agent.	Ref. 36
		Eggs	Decrease absorption. Yolk causes protein binding and reduced absorption.	Ref. 37
		Ascorbic acid	Increases absorption - should be avoided.	
^{99}Mo	Inhalation Ingestion Injection	$MgSO_4$ or Na_2SO_4 Cabbage rich in sulfate	Sulfate limits retention by reducing absorption and increasing urinary excretion.	Ref. 38

Table 2 (Cont'd)
Manipulations Possibly Useful in Preventing
Uptake of Radionuclides

RADIONUCLIDE	ROUTE OF ENTRY	MEDICATION OR DIETARY MANIPULATION	MECHANISM	COMMENTS
^{75}Se	Injection Ingestion	2% sodium sulfate in diet	Increases Se excretion threefold.	Ref. 39
^{65}Zn	Inhalation Ingestion Injection	Copper interferes with zinc uptake.	Proven in animals.	Ref. 40
		Phytates reduce uptake.	Proven in animals.	Ref. 41

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